Left atrial appendage function during DDD and VVI pacing

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Abstract

***Objective*—To examine, using transoesophageal echocardiography, the possible disturbances of left atrial appendage function during VVI and DDD pacing in patients with a normal atrium paced with a dual chamber system.**

***Design*—Randomised controlled trial.**

***Setting*—Tertiary care centre.**

***Patients*—22 patients (mean age 68 (SD 6) years) who had been paced with dual chamber pacemakers for at least six months. Exclusion criteria were valvar disease, cardiomyopathy, hypertension, and diabetes mellitus.**

***Interventions*—All patients underwent a transoesophageal echocardiographic evaluation of left atrial appendage function under DDD and VVI modes in random order. Measurements were made after at least two months' pacing in each mode.**

***Main outcome measures*—Echocardiographic indices of left atrial appendage flow under both pacing modes.**

***Results*—All 22 patients had higher emptying and filling flow velocities under DDD than under VVI mode. The filling and emptying flow velocity integrals were also significantly higher under DDD mode ($P < 0{\cdot}001$, $P = 0{\cdot}019$).**

***Conclusions*—Left atrial appendage function, as reflected in indices of emptying and filling assessed by transoesophageal echocardiography, is significantly different with DDD than with VVI pacing. This may explain the higher incidence of thromboembolic episodes in patients paced under VVI mode.**

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Keywords: left atrial appendage; transoesophageal echocardiography; thromboembolic events; pacing mode

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Although ventricular pacing is known to be associated with an increased incidence of systemic embolic episodes,[1–3] no precise pathophysiological mechanism has yet been shown to explain this. The left atrial appendage is a common site for the formation of thrombi, and reduced flow in the appendage predisposes to thrombus production in this region both during atrial fibrillation and during sinus rhythm.[4]

In the few published reports dealing with left atrial appendage function under various pacing modes[5 6] it has been shown that during VVI pacing the velocity of flow in the appendage is significantly reduced, especially in patients with atrial fibrillation and in those with ventriculoatrial conduction.

The aim of this study was to shed more light on this subject by comparing left atrial appendage function in the same patients following pacing under DDD and VVI modes. Other questions, such as the role of ventriculoatrial conduction, were also addressed in the study.

Methods

We studied 22 patients (12 men, 10 women; mean age 68 (SD 6) years) who had been paced with dual chamber systems for at least six months. Twelve of the patients had been paced for complete AV block, while the other 10 had sick sinus syndrome. Patients with enlarged cardiac chambers, heart failure of systolic or diastolic origin (New York Heart Association class II or more), valvar disease, ischaemic heart disease (diagnosed by thallium stress test), a history of atrial fibrillation, diabetes mellitus, or hypertension were excluded from the study.

All patients underwent a transoesophageal echocardiographic examination during pacing under VVI and DDD mode to evaluate left atrial appendage function. Patients were assigned to one of the two pacing modes with the help of an SPSS random number generating procedure and were paced under this mode for at least two months before the echo examination. The pacing mode was then switched and left for another two months before the echo examination was repeated.

The findings from the 22 patients were compared with those from a control group of 15 individuals, of similar age and sex distribution, with no evidence of heart disease, who also underwent a transoesophageal echocardiographic examination to exclude a cardiac source of thromboembolism.

PACING METHODS

The pacing rate was chosen on the same basis—for all patients and for both pacing modes—as the lowest rate which ensured continuous right atrial pacing under DDD mode. The AV delay chosen under DDD mode, based on the pacing rate and especially in those patients with sick sinus syndrome, was that which combined continuous ventricular capture and the highest cardiac output, as

Table 1 Transthoracic echocardiographic data from the patients and controls. Values are mean (SD)

	Patients	*Controls*	*P*
LVEDD (mm)	48 (4)	47 (3·5)	NS
LVESD (mm)	33 (4)	33·5 (3·5)	NS
LA(mm)	36 (5)	34 (4)	NS
PW (mm)	10 (0·5)	9·5 (1·0)	NS
IVS (mm)	9 (1)	10 (0·5)	NS
EF (%)	60 (10)	63 (9)	NS

LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LA, left atrium; PW, posterior wall; IVS, interventricular septum; EF, ejection fraction.

determined by the echocardiographic measurements from the left ventricular outflow tract. During VVI pacing we looked for ventriculoatrial conduction using intracavity recording by pacemaker telemetry.

ECHOCARDIOGRAPHIC STUDY

The transthoracic echocardiogram was recorded using a 2·5 MHz phased array transducer, while the transoesophageal study employed a 5 MHz biplane transducer (Hewlett Packard Sonos 1000 system). The latter examination was performed after the patients had fasted for at least four hours and following the administration of 25 mg meperidine hydrochloride. Local pharyngeal and hypopharyngeal anaesthesia was achieved with a 1% lignocaine spray. Sedation with 1–2 mg midazolame hydrochloride was used in five of the patients.

The examination was carried out with the patient in a left lateral position, using transverse sectional visualisation of the left atrial appendage at the level of the aortic valve, and the long axis two chamber view. The view which gave the clearest and most accurate picture was used for the evaluation of left atrial appendage flow velocity. The appendage flow was recorded using pulsed Doppler, with the sample volume just inside the appendage at a point where ghost signals due to wall motions were minimal. The maximum filling and emptying flow velocities, total filling and emptying flow velocity integrals, and the appendage filling and emptying times were measured for the two waveforms of left atrial appendage flow (inflow-filling and outflow-emptying, on both sides of a QRS with biphasic or quadriphasic morphology).

The entire study was recorded on VHS videotapes and the measurements were made later by two independent observers. Each variable was calculated as an average over 10 successive cardiac cycles.

STATISTICAL ANALYSIS

Data are expressed as mean (SD). Comparison between DDD and VVI modes was performed using the paired t test or Wilcoxon's signed rank test, as appropriate. Comparisons according to the presence or absence of ventriculoatrial conduction were made using the unpaired t test. A P value $< 0{\cdot}05$ was considered as significant.

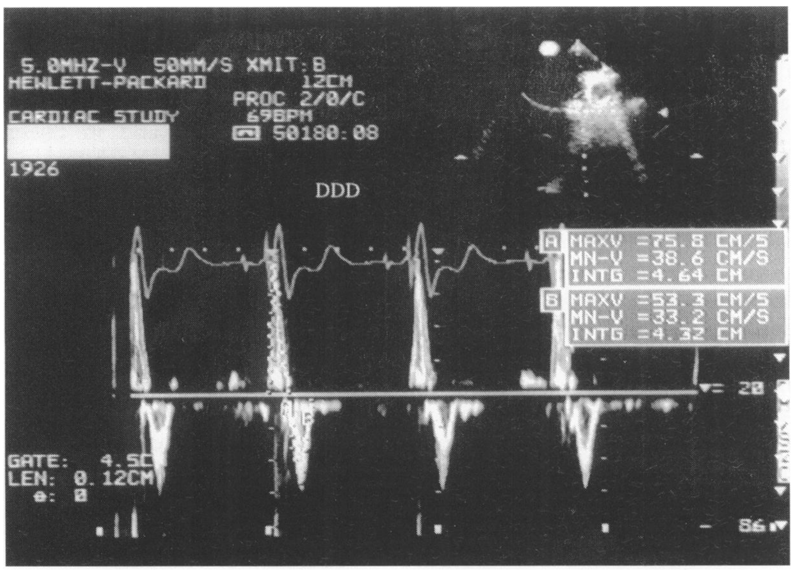

Figure 1 Pulsed wave Doppler recording showing left atrial appendage (LAA) flow under DDD pacing mode.

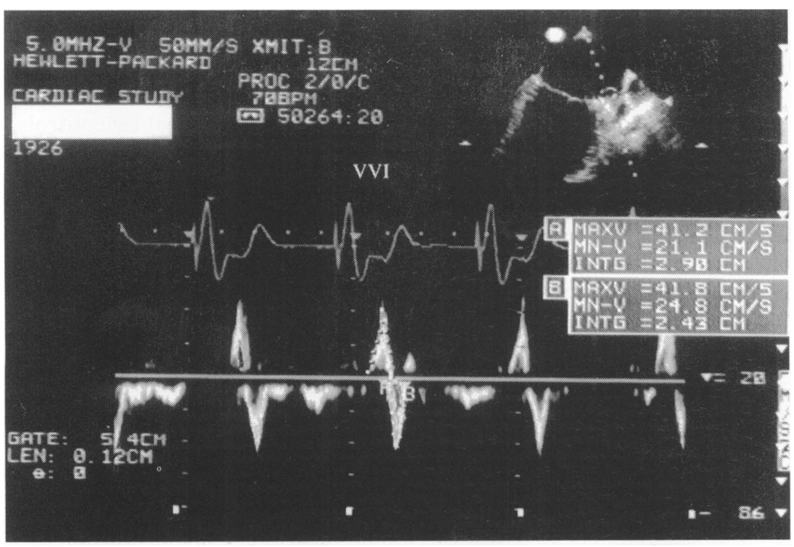

Figure 2 Pulsed wave Doppler recording showing left atrial appendage (LAA) flow under VVI pacing mode.

Results

The mean pacing rate which achieved stable pacing of the atria was 65 (4) beats/min under DDD mode and did not differ significantly from the mean rate under VVI (63 (3) beats/min). Eight patients had ventriculoatrial conduction during the study.

The transthoracic echocardiographic data from the patients and controls are shown in table 1. There were no significant differences between the groups.

Emptying (E) and filling (F) flow velocities, the flow velocity integrals of emptying and filling waves (IE and IF), and the emptying and filling times (TE and TF) were compared for the 22 patients paced under DDD and VVI modes. Figures 1 and 2 show examples of pulsed wave Doppler recordings of left atrial appendage flow under DDD and VVI pacing modes, respectively.

Table 2 shows the mean values of the above variables. Emptying and filling flow velocities were greater under DDD mode ($P < 0{\cdot}001$ for both)—all 22 patients had higher emptying

Table 2 Left atrial appendage flow variables under DDD and VVI pacing. Values are mean (SD)

	DDD	VVI	P
E (cm/s)	61·66 (7·88)	42·83 (11·23)	< 0·001
F (cm/s)	54·80 (10·79)	38·93 (10·23)	< 0·001
IE (cm)	4·22 (0·69)	2·82 (0·65)	< 0·001
IF (cm)	4·07 (1·07)	3·02 (1·70)	0·019
TE (ms)	116·46 (8·69)	109·46 (13·62)	0·10
TF (ms)	121·54 (18·68)	110·77 (18·64)	0·009

E, emptying velocity; F, filling velocity; IE, time velocity integral of emptying; IF, time velocity integral of filling; TE, emptying time; TF, filling time.

Table 3 Left atrial appendage flow variables under VVI pacing in patients with (+) and without (−) ventriculoatrial conduction (RAVC). Values are mean (SD). No significant differences were observed

	VVI/RAVC (+)	VVI/RAVC (−)
E (cm/s)	43·18 (5·17)	42·69 (13·16)
F (cm/s)	38·00 (6·35)	39·34 (11·88)
IE (cm)	2·79 (0·32)	2·84 (0·76)
IF (cm)	2·67 (0·21)	3·16 (2·03)
TE (ms)	115·00 (5·77)	107·00 (15·60)
TF (ms)	122·50 (22·17)	105·56 (15·41)

E, emptying velocity; F, filling velocity; IE, time velocity integral of emptying; IF, time velocity integral of filling; TF, emptying time; TF, filling time.

and filling flow velocities under DDD than under VVI mode. IE and IF were also higher under DDD ($P < 0{\cdot}001$, $P = 0{\cdot}019$). All patients had higher IE and all but one had higher IF under DDD. Emptying time was also higher under DDD but the difference did not reach statistical significance. Filling time was higher under DDD ($P = 0{\cdot}009$); 17 patients had higher values under DDD than under VVI.

Table 3 shows the mean values of the above variables in the 14 patients without and the eight with ventriculoatrial conduction during VVI pacing. There were no statistically significant differences between the two subgroups.

Having established the superiority of DDD mode, we compared the above variables with the values measured in normal subjects. While DDD pacing had a beneficial effect on the emptying and filling velocities, they still fell significantly short (by about 10 cm/s) of those found in normal subjects (table 4). Patients under DDD pacing did not differ significantly from normal subjects for IF ($P = 0{\cdot}058$). Neither emptying time nor filling time differed significantly between DDD paced patients and normal controls.

Discussion

Ventricular pacing, as opposed to atrial or atrioventricular pacing, has been associated with an increased incidence of thromboembolic episodes, which may occasionally occur even in the absence of atrial fibrillation. This finding has been confirmed by several retrospective studies,[2 3] while in a recent prospective randomised study Andersen *et al*,[1] comparing thromboembolic events in patients with sinus node disease paced under either AAI or VVI mode, found that ventricular pacing was the only variable significantly associated with an increased risk of thromboembolic events during follow up. The authors recommend anticoagulant treatment for patients paced under VVI mode in cases where it is not feasible to upgrade the pacing system.

In spite of the above observations, however, the precise mechanism leading to the thromboembolic events in these patients remains obscure. There has been a great deal of speculation about whether the left atrial appendage is a focus of thrombus formation, and it has also been shown that increased thrombogenesis is connected with poor contraction and dilatation in this structure.[4]

VVI pacing is known to affect the cardiac loading conditions,[7-9] which in turn—as Hoit *et al* have shown[10]—cause variations in the function of the left atrial appendage. In a recent study, Asanuma *et al*[5] found that the left atrial appendage flow velocity under VVI pacing was significantly reduced in patients with chronic atrial fibrillation and in those with ventriculoatrial conduction. Yoshitomi *et al*[6] also reported recently that the peak left atrial appendage flow velocity in 16 patients with dual chamber pacemakers was lower under VVI than under DDD mode, at 34 (18) *v* 52 (18) cm/s, $P < 0{\cdot}01$. These investigators concluded that impaired left atrial appendage function during VVI pacing may predispose to thrombus formation and to the formation of emboli.

In our present study we examined 22 patients using transoesophageal echocardiography to compare systolic and diastolic left atrial appendage function under DDD and VVI pacing, in random order, after at least two months' pacing under each mode. This length of time was allowed because little is known about the effects of extended pacing on left atrial appendage function, as opposed to the short term pacing employed in the study of Yoshitomi *et al*.[6] Our findings from patients paced under the two pacing modes were also compared with those from 15 healthy controls. We showed that left atrial appendage emptying and filling velocities, flow velocity integrals, and emptying and filling times were lower in patients with VVI pacing than in those with DDD pacing or in the control group. These variables were chosen as giving the best indications of left atrial appendage function.[11] The DDD pacing mode led to lower flow velocities than were found in the controls, although there were no significant differences between these two groups with regard to flow velocity integrals or emptying and filling times. However, in contrast to Asanuma *et al*,[5] we found no difference in the left atrial appendage flow velocity during VVI pacing between patients with and without ventriculoatrial conduction, although the small

Table 4 Left atrial appendage flow variables under DDD pacing and in normal subjects. Values are mean (SD)

	DDD	Normal	P
E (cm/s)	61·66 (7·88)	72·70 (8·50)	0·006
F (cm/s)	54·80 (10·79)	67·10 (5·08)	0·007
IE (cm)	4·22 (0·69)	4·55 (0·65)	0·290
IF (cm)	4·07 (1·07)	4·94 (0·75)	0·058
TE (ms)	116·46 (8·69)	107·00 (13·86)	0·068
TF (ms)	121·54 (18·68)	116·00 (11·60)	0·490

E, emptying velocity; F, filling velocity; IE, time velocity integral of emptying; IF, time velocity integral of filling; TE, emptying time; TF, filling time.

number of affected patients in our study limits the significance of this finding.

In conclusion, although DDD pacing did not have a significant adverse effect on left atrial appendage flow, VVI pacing in patients in sinus rhythm and without any organic heart disease caused LAA dysfunction regardless of the presence or absence of ventriculoatrial conduction. This dysfunction probably creates conditions for increased thrombogenesis and could thus increase the risk of systemic embolic episodes.

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